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Elevated Nicotine Levels in Cervical Lavages from Passive Smokers

Carol J. Jones, PhD, Mark H. Schiffman, MD, MPH, Robert Kurman, MD, Peyton Jacob III, PhD, and Neal L. Benowitz, MD

ABSTRACT

One hundred forty-five nonsmokers found to have normal cytologic diagnoses on routine Pap smears were interviewed regarding environmental exposure to tobacco smoke, and a 3 ml saline lavage of the cervix was collected for measurement of cervical nicotine levels by gas chromatography-mass spectroscopy. Nicotine levels tended to be highest among women exposed to tobacco smoke in the home, intermediate in women exposed only outside the home, and lowest in women recalling no exposure ($p = 0.001$). (*Am J Public Health* 1991;81:378–379)

Introduction

Women exposed to environmental tobacco smoke show biochemical evidence of smoke absorption in their saliva, serum, and urine.[1] A study of four women[2] recently reported that the cervical mucus of passive smokers might contain nicotine and its major metabolite, cotinine, concordant with the finding of increased concentrations of nicotine and cotinine in the cervical mucus of active smokers.[3,4] To confirm this report, we measured the concentrations of nicotine in cervical lavages taken from 145 cytologically normal, nonsmoking women, comparing concentrations in women passively exposed to tobacco smoke with those not exposed.

Methods

Subjects were part of a larger study of cervical neoplasia conducted in three Washington, DC area hospitals.[5] One hundred forty-five nonsmokers found to have normal cervical cytologic diagnoses on routine Pap smears were interviewed regarding environmental exposure to tobacco smoke, and a 3 ml saline lavage of the cervix was collected as previously described.[4] The interview included questions on the following topics: exposure to environmental tobacco smoke inside and outside the home in the previous 24 hours, time since last exposure, number of active smokers in the home, the smokers' relationship to the subject, and their usual intensity of smoking and products smoked (cigarette, cigar, pipe). The questionnaire focused on the 24 hours preceding specimen collection because previous research had indicated that cervical nicotine levels were correlated with active smoking during this period.[4] Specimens were kept frozen at −70° C until tested. All laboratory analyses were performed without knowledge of the smoking histories.

Nicotine was extracted from lavage samples by a modification of a published procedure.[6] The extracts were analyzed by combined gas chromatography-mass spectroscopy,[7] using a stable isotope-labeled analog, nicotine-d_4, as an internal standard. As a quality control measure, 17 aliquots of a pool composed of 19 cervicovaginal saline lavages, 17 from nonsmokers and two from smokers, were included among the specimens to be analyzed, with labels indistinguishable from the test specimens. The quality control data suggested that nicotine was measured reliably in the lavages. The mean of the 17 replicate measurements was 2.72 ng/ml with a coefficient of variation of 13.6 percent and a range of 2.2–3.5 ng/ml.

To classify subjects with regard to environmental tobacco smoke exposure, the following categories were formed: group 1 included women who reported exposure inside their homes within the past 24 hours, group 2 was comprised of women reporting exposure only outside their homes within the past 24 hours, and group 3 included women who recalled no exposure to environmental tobacco smoke in the previous 24 hours.

Address reprint requests to Mark H. Schiffman, MD, MPH, Environmental Epidemiology Branch, National Cancer Institute, Executive Plaza North 443, Bethesda, MD 20892. Dr. Jones is also with EEB/NCI; Dr. Kurman is with Georgetown University Hospital; Drs. Jacob and Benowitz are with the University of California at San Francisco. This paper, submitted to the Journal December 15, 1989, was revised and accepted for publication September 5, 1990.

TABLE 1—Nicotine Levels in Cervical Lavages from 145 Nonsmokers, according to Exposure to Environmental Tobacco Smoke over the past 24 Hours

Nicotine level (ng/ml)	Group 1 (exposed at home)		Group 2 (exposed only outside home)		Group 3* (not exposed)	
	#	%	#	%	#	%
<0.2	5	15.6	6	14.3	22	31.4
0.2–0.3	7	21.9	14	33.3	21	30.0
0.4–0.7	4	12.5	10	23.8	20	28.6
>0.7	16	50.0	12	28.6	7	10.0
Total	32	100.0	42	100.0	70	100.0

Chi-square = 22.5, 6 degrees of freedom, p = 0.001
*Group 3 excludes one woman with an inadequate specimen.

Results

The study population was predominantly Black (63.5 percent); the median age was 30 years (range 16–66). Neither age nor race was associated with environmental tobacco smoke exposure.

A total of 32 women reported exposure to environmental tobacco smoke in the home (group 1), 42 reported exposure only outside the home (group 2), and 71 were unexposed (group 3). In group 1, 24 reported one active smoker in the home, five reported two active smokers, and three reported three or more active smokers in the home. Seven in group 1 recalled additional exposure to tobacco smoke outside the home.

Nicotine values ranged from below the limit of detection (<0.2 ng/ml) to 8.2 ng/ml. Nicotine levels tended to be highest among women in group 1 (exposed in the home), intermediate in group 2 (exposed only outside the home), and lowest in group 3 (not exposed). The median values for the three groups were: group 1, 0.8 ng/ml (range, <0.2–8.2), group 2, 0.4 ng/ml (range <0.2–5.2), and group 3, 0.2 ng/ml (range <0.2–3.8).

For grouped analysis, the nicotine levels were divided into approximate quartiles as shown in Table 1. The association of recalled environmental tobacco smoke exposure in the past 24 hours and detectable nicotine in cervical lavages was highly significant (p = 0.001).

Among the 38 women with exposure at home in the past 24 hours, there was no association observed between nicotine levels and the number of smokers to whom the women had been exposed, the usual smoking intensity of those active smokers, or the number of hours since last exposure. Moreover, for women exposed to smoke in the home, additional exposure outside the home was not related to nicotine level. Cigarette smoke accounted for virtually all of the exposure at home. Among women exposed only outside the home, there was no relationship observed between time since last exposure to environmental tobacco smoke and nicotine level.

Discussion

We observed a significant association between self-reported exposure to environmental tobacco smoke within the previous 24 hours and nicotine levels in cervical lavages from a group of 145 nonsmoking women. Exposure in the home resulted in the highest nicotine levels observed; however, women exposed only outside the home also had elevated levels of nicotine compared to those not exposed.

The biological significance of cervical nicotine levels resulting from passive exposure to tobacco smoke is not known. The levels of nicotine observed in nonsmokers most heavily exposed in our population were on average much lower than those seen in cervical lavages taken from active smokers. We found the median nicotine level in nonsmoking women exposed to environmental tobacco smoke at home to be 0.8 ng/ml (mean 1.1), ranging up to 8.2 ng/ml. We were unable to relate nicotine levels to more subtle distinctions, such as the intensity of home exposure. In contrast, using similar specimen collection and analytic methods, we observed a median value in 31 active smokers of 11.8 ng/ml (mean 34.3, range 2.8–383.4, unpublished data) and were able to correlate increasing intensity of active smoking with increasing cervical nicotine levels (Spearman's r = 0.46, p = 0.009). It is difficult to reconcile the relatively low levels of nicotine that we observed in passive smokers with the large magnitude of the relative risks reported by Slattery, *et al,* who found a risk from passive smoking similar to that of actively smoking women.[8]

It is remarkable, nonetheless, that even a relatively crude exposure categorization provided by questionnaire responses revealed a clear, albeit small, elevation of nicotine levels in the cervical fluid of passive smokers. This supports the idea that even low-level exposure to tobacco smoke in the environment may result in systemic effects, and suggests that passive smoking should be evaluated further as a risk factor for cervical disease. □

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